

WHAT IS CLAIMED IS:

1. A method for identifying markers for a human disease state, comprising the following steps:

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- a) providing human peripheral blood mRNAs;
- b) amplifying said mRNAs to provide nucleic acid amplification products;
- 10 c) separating said nucleic acid amplification products; and
- d) identifying those mRNAs that are differentially expressed between normal individuals and individuals exhibiting said disease state.

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2. The method defined in claim 1, further described as comprising the step of converting said RNAs into cDNAs using reverse transcriptase.

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3. The method defined in claim 2, further comprising using random hexamers, arbitrarily chosen oligonucleotides, promiscuous oligonucleotide primers or anchoring primers for the reverse transcription step.

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4. The method defined in claim 3, further comprising using said arbitrarily chosen oligonucleotides, promiscuous oligonucleotide primers and/or anchoring primers for the amplification step.

5. The method defined in claim 1, wherein the disease state is metastatic or organ confined cancer, asthma, lupus erythromatosis, rheumatoid arthritis, multiple sclerosis, myasthenia gravis, autoimmune thyroiditis, ALS (Lou Gehrig's disease), interstitial cystitis or prostatitis.

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6. The method defined in claim 5, wherein the disease state is metastatic prostate cancer.

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7. The method defined in claim 5, wherein the disease state is metastatic breast cancer.

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8. A method of detecting a human disease state, comprising the steps of:

a) detecting the quantity of a disease marker expressed in human peripheral blood; and

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b) comparing the quantity of said marker to the quantity expressed in peripheral blood of a normal individual;

wherein a difference in quantity of expression is indicative of a disease state.

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9. The method of claim 8, wherein said disease marker is an mRNA.

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10. The method of claim 9, wherein said mRNA is amplified by an RNA polymerase reaction.

11. The method of claim 9, wherein said mRNA is amplified by reverse transcriptase polymerase chain reaction or the ligase chain reaction.

5 12. The method of claim 8, wherein said detecting is by RNA fingerprinting, branched DNA or a nuclease protection assay.

10 13. The method of claim 8, wherein the disease state is metastatic cancer, asthma, lupus erythromatosis, rheumatoid arthritis, multiple sclerosis, myasthenia gravis, autoimmune thyroiditis, ALS (Lou Gehrig's disease), interstitial cystitis or prostatitis.

15 14. The method of claim 8 wherein the disease state is metastatic cancer.

15 15. The method of claim 14 wherein the metastatic cancer is metastatic prostate cancer.

20 16. The method of claim 14 wherein the metastatic cancer is metastatic breast cancer.

25 17. The method of claim 9 in which said mRNA comprises one or more of the sequences or the complements of the sequences disclosed herein as SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:29, SEQ ID NO:34, SEQ ID NO:48 or SEQ ID NO:49.

18. The method of claim 8 in which said marker is a product of an interleukin 8 (IL-8) or interleukin 10 (IL-10) gene.

5 19. The method of claim 9, further comprising the steps of

a) providing primers that selectively amplify said disease state marker;

b) amplifying said nucleic acid with said primers to form nucleic acid
10 amplification products;

c) detecting said nucleic acid amplification products; and

d) measuring the amount of said nucleic acid amplification products formed.
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20. The method of claim 19 in which said primers are selected to specifically amplify a nucleic acid having a sequence comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:29, SEQ ID NO:34, SEQ ID NO:48 or SEQ ID NO:49.
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21. The method of claim 8, wherein said marker is a polypeptide.

25 22. The method of claim 21, wherein said polypeptide is encoded by a nucleic acid sequence comprising the sequence disclosed herein SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:29, SEQ ID NO:34, SEQ ID NO:48 or SEQ ID NO:49.

23. The method of claim 21, wherein said detection is by an antibody immunoreactive with said marker.

5 24. The method of claim 21, wherein said polypeptide is encoded by an IL-8 or IL-10 gene.

10 25. The method of claim 8, wherein said marker is a product of the IL-8 gene and wherein said comparison is between two alternatively spliced forms of an IL-8 gene product.

15 26. The method of claim 24, wherein the quantity of IL-8 polypeptide in peripheral blood is measured using an *in vitro* bioassay that detects an IL-8 mediated biological process.

20 ~~27. A method for treating a subject with cancer comprising the steps of:~~
~~(i) providing an antisense expression construct comprising a nucleic acid, wherein the RNA expressed from said nucleic acid binds under high stringency conditions to a nucleic acid comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:29 or SEQ ID NO:34, and a promoter functional in eukaryotic cells wherein said nucleic acid is under transcriptional control of said promoter; and~~
~~25 (ii) contacting said expression construct with peripheral leukocyte cells of said subject in a manner that allows the uptake of said expression construct by said cells.~~

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28. The method of claim 27, wherein expression of said nucleic acid results in the modification of the immune response of said peripheral leukocyte cells to said cancer.

29. The method of claim 25 wherein said markers comprise SEQ ID NO:2 and SEQ ID NO:3.

~~30.~~ A kit for use in detecting a human disease comprising:

(a) a pair of primers for amplifying a disease state marker consisting of a nucleic acid; and

(b) containers for each of said primers.

31. A kit according to claim 30 in which the pair of primers is selected to amplify a nucleic acid marker for metastatic human cancer.

32. A kit according to claim 31 in which the pair of primers is selected to amplify a nucleic acid having a sequence comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:29, SEQ ID NO:34, SEQ ID NO:48 or SEQ ID NO:49.

33. A kit according to claim 31, comprising:

(a) a pair of primers selected to amplify a nucleic acid sequence comprising SEQ ID NO:2; and

(b) a pair of primers selected to amplify a nucleic acid sequence comprising SEQ ID NO:3.

5 34. A kit for use in diagnosing metastatic cancer in a biological sample, comprising:

(a) an antibody which binds with high specificity to a polypeptide having an amino acid sequence encoded by a nucleic acid sequence comprising SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:29, SEQ ID NO:34, SEQ ID NO:48 or SEQ ID NO:49; and

(b) a container for said antibody.

15 35. A kit according to claim 32, further defined as comprising:

(a) an antibody that binds with high specificity to a soluble IL-8 gene product;

(b) an antibody that binds with high specificity to a membrane bound IL-8 gene product; and

(c) a container for each antibody.

25 36. A kit according to claim 34, wherein said metastatic cancer is metastatic prostate cancer.

37. A method of detecting prostate cancer in a biological sample, comprising:

(a) measuring the levels of IL-8 or IL-10 in combination with at least one prostate disease marker in said sample; and

(b) comparing said levels with corresponding levels obtained from reference populations of normal individuals, individuals with BPH and individuals with prostate cancer.

38. The method of claim 37 in which said prostate disease marker is selected from a group consisting of total prostate specific antigen (PSA); prostate specific membrane antigen (PSMA=Folic Acid Hydrolase); prostate acid phosphatase (PAP); prostatic secretory proteins (PSP₉₄); human kallekrein 2 (HK2); and the ratio of the concentrations of free and bound forms of PSA (f/t PSA).

39. The method of claim 38, in which the biological sample comprises peripheral human blood.

40. The method of claim 39, wherein the level of IL-8 in a biological sample is measured using at least one antibody that binds to an IL-8 gene product.

41. The method of claim 40, wherein the level of IL-8 gene product bound to antibody is measured by ELISA.

42. The method of claim 39, wherein the level of IL-8 in a biological sample is measured using at least one oligonucleotide probe that binds to an IL-8 messenger RNA (mRNA).

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43. The method of claim 42, wherein an IL-8 mRNA is alternatively spliced to include intron 3.

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44. The method of claim 42, wherein the level of oligonucleotide probe bound to IL-8 mRNA is measured by nuclease protection assay.

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45. The method of claim 42, wherein the level of oligonucleotide probe bound to IL-8 mRNA is measured by RT-PCR™.

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46. The method of claim 42, wherein the level of oligonucleotide probe bound to IL-8 mRNA is measured by ligase chain reaction.

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47. The method of claim 42, wherein the level of oligonucleotide probe bound to IL-8 mRNA is measured by PCR™.

48. The method of claim 39, wherein the level of IL-8 in a biological sample is measured using an *in vitro* bioassay that detects an IL-8 mediated biological process.

49. The method of claim 39, wherein the level of IL-8 in a biological sample is measured using at least one molecule that binds to an IL-8 gene product, wherein said molecule is selected from a group consisting of: an IL-8 binding protein; and an IL-8 receptor protein.

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50. The method of claim 38, wherein the level of prostate disease marker in a biological sample is measured using at least one antibody that binds to at least one prostate disease marker protein.

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51. The method of claim 50, wherein the level of prostate disease marker protein bound to antibody is measured by ELISA.

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52. The method of claim 38, wherein the level of prostate disease marker in a biological sample is measured using at least one oligonucleotide probe that binds to at least one prostate disease marker messenger RNA (mRNA).

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53. The method of claim 42, wherein the level of oligonucleotide probe bound to prostate disease marker mRNA is measured by nuclease protection assay.

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54. The method of claim 42, wherein the level of oligonucleotide probe bound to prostate disease marker mRNA is measured by RT-PCR™.

55. The method of claim 42, wherein the level of oligonucleotide probe bound to prostate disease marker mRNA is measured by ligase chain reaction.

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57. The method of claim 42, wherein the level of oligonucleotide probe bound to prostate disease marker mRNA is measured by PCR™.

5 58. A method of differentially diagnosing prostate cancer and benign prostatic hyperplasia comprising the step of measuring the levels of IL-8 or IL-10 in combination with at least one prostate disease marker in a biological sample.

10 59. The method of claim 58 in which said prostate disease marker is selected from a group consisting of: total prostate specific antigen (PSA), prostate specific membrane antigen (PSMA=Folic Acid Hydrolase), prostate acid phosphatase (PAP), prostatic secretory proteins (PSP₉₄), human kallekrein 2 (HK2), and the ratio of the concentrations of free and bound forms of PSA (f/t PSA).

15 60. The method of claim 58, in which said biological sample consists of peripheral human blood.

20 61. A kit for detecting or differentially diagnosing human prostate cancer comprising:

(a) at least one detection agent for measuring the levels of IL-8 or IL-10 in a biological sample;

25 (b) at least one detection agent for measuring the levels of at least one prostate disease marker in said biological sample; and

(c) containers for each of said detection agents.

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62. The kit of claim 61 in which said prostate disease marker is selected from a group consisting of total prostate specific antigen (PSA), prostate specific membrane antigen (PSMA=Folic Acid Hydrolase), prostate acid phosphatase (PAP), prostatic secretory proteins (PSP₉₄), human kallekrein 2 (HK2), and the ratio of the concentrations of free and bound forms of PSA (f/t PSA).

63. The kit of claim 62 in which said detection agents are selected from a group consisting of polyclonal antibodies; monoclonal antibodies; oligonucleotides; paired oligonucleotides designed to bind to opposite strands of a double-stranded DNA molecule; and at least one molecule that binds to an IL-8 gene product.

64. The method of claim 19, in which said primers are selected to specifically amplify a nucleic acid product of the IL-10 gene.

65. The method of claim 24, wherein the quantity of IL-10 polypeptide in peripheral blood is measured using an *in vitro* bioassay that detects at least one IL-10 mediated biological process.

66. A method for treating a subject with cancer comprising the steps of:

(i) providing an antisense expression construct comprising a nucleic acid, wherein the RNA expressed from said nucleic acid binds under high stringency conditions to an RNA product of the IL-8 or IL-10 genes, and a promoter functional in eukaryotic cells wherein said nucleic acid is under transcriptional control of said promoter; and

- (ii) contacting said expression construct with peripheral leukocyte cells of said subject in a manner that allows the uptake of said expression construct by said cells.

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67. The method of claim 66, wherein expression of said nucleic acid results in the modification of the immune response of said peripheral leukocyte cells to said cancer.

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68. A kit according to claim 31, comprising a pair of primers selected to amplify a nucleic acid sequence encoded by an IL-10 gene.

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69. The method of claim 39, wherein the level of IL-10 in a biological sample is measured using at least one antibody that binds to an IL-10 gene product.

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70. The method of claim 69, wherein the level of IL-10 gene product bound to antibody is measured by ELISA.

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71. The method of claim 39, wherein the level of IL-10 in a biological sample is measured using at least one oligonucleotide probe that binds an IL-10 messenger RNA (mRNA).

~~72.~~ An isolated nucleic acid segment having a sequence consisting essentially of SEQ ID NO:49 or its complement.

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